Table 1H-1. *Streptococcus* spp. β-Hemolytic Group

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Clindamycin[a,b]			
Erythromycin[a,b,c]			
Penicillin[d] or ampicillin[d]		Cefotaxime or ceftriaxone	Cefepime
			Ceftaroline
	Tetracycline		
		Vancomycin	
			Linezolid
			Tedizolid[e]
			Daptomycin[f,g]
			Levofloxacin
			Dalbavancin[g,h]
			Oritavancin[g]
			Telavancin[g]

Abbreviations: FDA, US Food and Drug Administration; ICR, inducible clindamycin resistance; MDRO, multidrug-resistant organism; MIC, minimal inhibitory concentration.

Table 1H-1. *Streptococcus* spp. β-Hemolytic Group (Continued)

Footnotes

a. Not routinely reported for organisms isolated from urinary tract.

b. ***Rx:*** Recommendations for intrapartum prophylaxis for group B streptococci are penicillin or ampicillin. Although cefazolin is recommended for penicillin-allergic women at low risk for anaphylaxis, those at high risk for anaphylaxis may receive clindamycin or vancomycin (if the isolate is not susceptible to clindamycin).[1] Group B streptococci are susceptible to ampicillin, penicillin, and cefazolin but may be resistant to erythromycin and clindamycin. When clindamycin is being considered for intrapartum prophylaxis (eg, pregnant woman with severe penicillin allergy), erythromycin and clindamycin (including ICR) should be tested, but only clindamycin should be reported. See Table 3J.

c. Susceptibility and resistance to azithromycin and clarithromycin can be predicted by testing erythromycin.

d. Penicillin and ampicillin are drugs of choice for treating β-hemolytic streptococcal infections. Susceptibility testing of penicillins and other β-lactams approved by the FDA for treatment of β-hemolytic streptococcal infections does not need to be performed routinely, because nonsusceptible isolates (ie, penicillin MICs > 0.12 and ampicillin MICs > 0.25 µg/mL) are extremely rare in any β-hemolytic streptococci and have not been reported for *S. pyogenes*. If testing is performed, any β-hemolytic streptococcal isolate found to be nonsusceptible should be re-identified, retested, and if confirmed, submitted to a public health laboratory (see Appendix A for additional instructions).

e. Report only on *S. pyogenes* and *S. agalactiae*.

f. Not routinely reported on organisms isolated from the lower respiratory tract.

g. MIC testing only; disk diffusion test is unreliable.

h. Report only on *S. pyogenes, S. agalactiae,* and *S. dysgalactiae*.

Reference for Table 1H-1

1 American College of Obstetricians and Gynecologists. Prevention of group B streptococcal early-onset disease in newborns: ACOG Committee Opinion, Number 797. *Obstet Gynecol*. 2020;135(2):e51-e72. doi:10.1097/AOG.0000000000003668

Table 2H-1. Zone Diameter and MIC Breakpoints for *Streptococcus* spp. β-Hemolytic Group

Testing Conditions

Medium: Disk diffusion: MHA with 5% sheep blood
Broth dilution: CAMHB with LHB (2.5% to 5% v/v); the CAMHB should be supplemented to 50 µg/mL calcium for daptomycin (see CLSI M07[1] for instructions for preparation of LHB).
Agar dilution: MHA with sheep blood (5% v/v); recent studies using the agar dilution method have not been performed and reviewed by the subcommittee.

Inoculum: Colony suspension, equivalent to a 0.5 McFarland standard, using colonies from an overnight (18- to 20-hour) sheep blood agar plate

Incubation: 35°C ± 2°C
Disk diffusion: 5% CO_2; 20–24 hours
Dilution methods: ambient air; 20–24 hours (CO_2 if necessary, for growth with agar dilution)

QC Recommendations

Refer to the following:

- **Tables 4B and 5B that list acceptable QC ranges applicable for each method**
- **Appendix I to develop a QC plan**

When a commercial test system is used for antimicrobial susceptibility testing, refer to the manufacturer's instructions for QC **strains** and QC ranges.

Refer to Table 3J for additional testing recommendations, reporting suggestions, and QC.

General Comments

(1) Refer to Table 1H-1 for antimicrobial agents that should be considered for testing and reporting by microbiology laboratories.

(2) For disk diffusion, test a maximum of 9 disks on a 150-mm plate and 4 disks on a 100-mm plate. Measure the diameter of the zones of complete inhibition (as judged by the unaided eye), including the diameter of the disk (see CLSI M02QG[2]). The zone margin should be considered the area showing no obvious, visible growth that can be detected with the unaided eye. Do not measure the zone of inhibition of hemolysis. Measure the zones from the upper surface of the agar illuminated with reflected light, with the cover removed. Ignore faint growth of tiny colonies that can be detected only with a magnifying lens at the edge of the zone of inhibited growth.

(3) For β-hemolytic streptococci when testing chloramphenicol, clindamycin, erythromycin, linezolid, tedizolid, and tetracycline by broth microdilution MIC, trailing growth can make end-point determination difficult. In such cases, read the MIC at the lowest concentration where the trailing begins. Tiny buttons of growth should be ignored (see CLSI M07[1]).

Table 2H-1. *Streptococcus* spp. β-Hemolytic Group (Continued)

(4) For this table, the β-hemolytic group includes the large colony–forming pyogenic strains of streptococci with group A (*S. pyogenes*), C, or G antigens and strains with Group B (*S. agalactiae*) antigen. Small colony–forming β-hemolytic strains with group A, C, F, or G antigens (*S. anginosus* group, previously *S. milleri*) are considered part of the viridans group, and breakpoints for the viridans group should be used (see Table 2H-2).

(5) Penicillin and ampicillin are drugs of choice for treating β-hemolytic streptococcal infections. Susceptibility testing of penicillins and other β-lactams approved by the FDA for treatment of β-hemolytic streptococcal infections does not need to be performed routinely, because nonsusceptible isolates (ie, penicillin MICs > 0.12 and ampicillin MICs > 0.25 µg/mL) are extremely rare in any β-hemolytic streptococci and have not been reported for *S. pyogenes*. If testing is performed, any β-hemolytic streptococcal isolate found to be nonsusceptible should be re-identified, retested, and, if confirmed, submitted to a public health laboratory. See Appendix A for additional instructions.

(6) Breakpoints for *Streptococcus* spp. β-hemolytic group are proposed based on population distributions of various species, pharmacokinetics of the antimicrobial agents, previously published literature, and the clinical experience of subcommittee members. Systematically collected clinical data were not available for review with many of the antimicrobial agents in this table.

NOTE: Information in boldface type is new or modified since the previous edition.

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
		S	I	R	S	I	R	
PENICILLINS								
(7) An organism that is susceptible to penicillin can be considered susceptible to antimicrobial agents listed here when used for approved indications and does not need to be tested against those agents. For groups A, B, C, and G β-hemolytic streptococci, penicillin is tested as a surrogate for ampicillin, amoxicillin, amoxicillin-clavulanate, ampicillin-sulbactam, cefazolin, cefepime, ceftaroline, cephradine, cephalothin, cefotaxime, ceftriaxone, ceftizoxime, imipenem, ertapenem, and meropenem. For group A β-hemolytic streptococci, penicillin is also a surrogate for cefaclor, cefdinir, cefprozil, ceftibuten, cefuroxime, and cefpodoxime.								
Penicillin or	10 units	≥ 24	–	–	≤ 0.12	–	–	See general comment (5).
ampicillin	10 µg	≥ 24	–	–	≤ 0.25	–	–	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)								
See comment (7).								
Cefepime or	30 µg	≥ 24	–	–	≤ 0.5	–	–	
cefotaxime or	30 µg	≥ 24	–	–	≤ 0.5	–	–	
ceftriaxone	30 µg	≥ 24	–	–	≤ 0.5	–	–	
Ceftaroline	30 µg	≥ 26	–	–	≤ 0.5	–	–	

Table 2H-1. *Streptococcus* spp. β-Hemolytic Group (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
		S	I	R	S	I	R	
CARBAPENEMS								
See comment (7).								
Doripenem*	–	–	–	–	≤ 0.12	–	–	
Ertapenem*	–	–	–	–	≤ 1	–	–	
Meropenem*	–	–	–	–	≤ 0.5	–	–	
GLYCOPEPTIDES								
Vancomycin	30 µg	≥ 17	–	–	≤ 1	–	–	
LIPOGLYCOPEPTIDES								
Dalbavancin	–	–	–	–	≤ 0.25	–	–	**(8)** Report only on *S. pyogenes, S. agalactiae,* and *S. dysgalactiae.*
Oritavancin	–	–	–	–	≤ 0.25	–	–	
Telavancin	–	–	–	–	≤ 0.12	–	–	
LIPOPEPTIDES								
Daptomycin	–	–	–	–	≤ 1	–	–	**(9)** Not routinely reported on organisms isolated from the lower respiratory tract.
MACROLIDES								
(10) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin. **(11)** Not routinely reported on organisms isolated from the urinary tract.								
Erythromycin	15 µg	≥ 21	16–20	≤ 15	≤ 0.25	0.5	≥ 1	**(12)** ***Rx:*** Recommendations for intrapartum prophylaxis for group B streptococci are penicillin or ampicillin. Although cefazolin is recommended for penicillin-allergic women at low risk for anaphylaxis, those at high risk for anaphylaxis may receive clindamycin or vancomycin (if the isolate is not susceptible to clindamycin).[3] Group B streptococci are susceptible to ampicillin, penicillin, and cefazolin but may be resistant to erythromycin and clindamycin. When clindamycin is being considered for intrapartum prophylaxis (eg, pregnant woman with severe penicillin allergy), erythromycin and clindamycin (including ICR) should be tested, but only clindamycin should be reported. See Table 3J.

Table 2H-1. *Streptococcus* spp. β-Hemolytic Group (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
		S	I	R	S	I	R	
MACROLIDES (Continued)								
Azithromycin*	15 µg	≥ 18	14–17	≤ 13	≤ 0.5	1	≥ 2	
Clarithromycin*	15 µg	≥ 21	17–20	≤ 16	≤ 0.25	0.5	≥ 1	
Dirithromycin*	15 µg	≥ 18	14–17	≤ 13	≤ 0.5	1	≥ 2	
TETRACYCLINES								
(13) Isolates that **test** susceptible to tetracycline are considered susceptible to doxycycline and minocycline.								
Tetracycline	30 µg	≥ 23	19–22	≤ 18	≤ 2	4	≥ 8	
FLUOROQUINOLONES								
Levofloxacin	5 µg	≥ 17	14–16	≤ 13	≤ 2	4	≥ 8	
Gatifloxacin*	5 µg	≥ 21	18–20	≤ 17	≤ 1	2	≥ 4	
Grepafloxacin*	5 µg	≥ 19	16–18	≤ 15	≤ 0.5	1	≥ 2	
Ofloxacin*	5 µg	≥ 16	13–15	≤ 12	≤ 2	4	≥ 8	
Trovafloxacin*	10 µg	≥ 19	16–18	≤ 15	≤ 1	2	≥ 4	
PHENICOLS								
Chloramphenicol*	30 µg	≥ 21	18–20	≤ 17	≤ 4	8	≥ 16	See comment (11).
LINCOSAMIDES								
Clindamycin	2 µg	≥ 19	16–18	≤ 15	≤ 0.25	0.5	≥ 1	See comments (11) and (12). **(14)** For isolates that test erythromycin resistant and clindamycin susceptible or intermediate, testing for ICR by disk diffusion using the D-zone test or by broth microdilution is required before reporting clindamycin. See Table 3J, CLSI M02,[4] and CLSI M07.[1]
STREPTOGRAMINS								
Quinupristin-dalfopristin*	15 µg	≥ 19	16–18	≤ 15	≤ 1	2	≥ 4	**(15)** Report only on *S. pyogenes*.

Table 2H-1. *Streptococcus* spp. β-Hemolytic Group (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, µg/mL			Comments
		S	I	R	S	I	R	
OXAZOLIDINONES								
(16) *S. agalactiae* and *S. pyogenes* that test susceptible to linezolid are considered susceptible to tedizolid. Isolates that **test** nonsusceptible to linezolid **should be tested against tedizolid if that result is needed for treatment.**								
Linezolid	30 µg	≥ 21	–	–	≤ 2	–	–	
Tedizolid	2 µg	≥ 15	–	–	≤ 0.5	–	–	**(17)** Report only on *S. pyogenes* and *S. agalactiae*.

Abbreviations: CAMHB, cation-adjusted Mueller-Hinton broth; CO_2, carbon dioxide; FDA, US Food and Drug Administration; I, intermediate; ICR, inducible clindamycin resistance; LHB, lysed horse blood; MHA, Mueller-Hinton agar; MIC, minimal inhibitory concentration; QC, quality control; R, resistant; S, susceptible.
Symbol: *, designation for "Other" agents not included in Tables 1 but have established clinical breakpoints.

References for Table 2H-1

1 CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 12th ed. CLSI standard M07. Clinical and Laboratory Standards Institute; 2024.

2 CLSI. *M02 Disk Diffusion Reading Guide*. 2nd ed. CLSI quick guide M02-Ed14-QG. Clinical and Laboratory Standards Institute; 2024.

3 American College of Obstetricians and Gynecologists. Prevention of group B streptococcal early-onset disease in newborns: ACOG Committee Opinion, Number 797. *Obstet Gynecol*. 2020;135(2):e51-e72. doi:10.1097/AOG.0000000000003668

4 CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 14th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2024.